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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/463,082	07/10/2000	CHENICHERI H. NAIR	5-00	5840
23713	7590	04/20/2004	EXAMINER	
GREENLEE WINNER AND SULLIVAN P C 5370 MANHATTAN CIRCLE SUITE 201 BOULDER, CO 80303			WELLS, LAUREN Q	
			ART UNIT	PAPER NUMBER
			1617	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/463,082	Applicant(s) NAIR ET AL.	
	Examiner Lauren Q Wells	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31,33-35,61,64,68,71 and 80-83 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31,33-35,61,64,68,71 and 80-83 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 31, 33-35, 61, 64, 68, 71, 80-83 are pending. The Amendment filed 11/14/03, amended claim 31, added claims 80-82, and cancelled claim 72.

The cancellation of claim 72 is sufficient to overcome the 35 USC 112 rejection over this claim in the previous Office Action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 31, 33, 34, 61, 71, 80-83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. (WO 93/15768) in view of The Handbook of Carbon, Graphite, Diamond, and Fullerenes, and in view of Reno et al. (5,217,705).

The instant invention is directed toward a method for the in vivo detection of fibrin, comprising administering to a patient an effective amount of a detectable reagent comprising discrete particles dispersed in a pharmaceutically or veterinarily acceptable carrier, diluent, excipient, adjuvant or any combination thereof, wherein said particles comprise a detectable marker encased in at least two layers of carbon, wherein the outer surface of said particles allows for a stable chemical association with an aqueous medium and wherein upon administration of said reagent said particles are dispersed in the aqueous medium and form a stable colloid; binding said particles to said fibrin; and detecting the presence of said detectable marker in said patient.

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Watson et al. teach the use of macromolecular compounds having tight molecular meshes, such as graphite carbons, in diagnostic and/or therapeutic agents, especially diagnostic imaging contrast agents. The compounds are useful as supports or surrounds for diagnostic or therapeutic entities. The skeleton structure of the compounds can be derivatized to enhance other properties of the macromolecule, such as hydrophilic or lipophilic groups, or biologically targeting groups or structures. Specific derivatization groups include proteins, antibodies, cell adhesion molecules and others. Solubilizing groups can be attached to the carbon skeleton, for example polyalkoxylated alkyl or alkoxy groups. A method of diagnostic imaging is taught, wherein an effective amount of a compound comprising a contrast agent in combination with a macromolecular compound is administered to a human. Administration to the circulatory system is taught, wherein the compound targets the blood pool. The compounds are taught in physiologically acceptable carriers in the form of dispersions, which are synonymous to colloids. The reference lacks binding to fibrin and two layers of carbon. See pg. 1, 3-12, 14, 23, 26-30.

The Handbook of carbon, Graphite, Diamond, and Fullerene teach graphite crystal as being in the form of multiple layers. See page 44.

Reno et al. teach a method of diagnosing blood clots using fibrin-binding proteins. The proteins are attached to detectable substances, such as radioisotopes of iodine, bromine, fluorine, or ^{99m}Tc . See Col. 5, lines 20-56.

It would have been obvious to one of ordinary skill in the art at the time the invention was made for Watson to teach the graphitic carbon as comprising two or more carbon layers because The Handbook of Carbon, Graphite, Diamond, and Fullerenes teaches graphitic carbon as being in the form of multiple layers.

While Watson does not explicitly exemplify graphitic carbon, it would have been obvious to one of ordinary skill in the art at the time the invention was made to exemplify graphitic carbon in substitution for fullerenes in the examples of Watson because Watson teaches graphitic carbon and fullerenes as interchangeable macromolecular compounds for use in his invention; thus, one of skill would be motivated to substitute one for the other because of the expectation of achieving equivalent imaging effects.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach fibrin-binding proteins, as taught by Reno et al., as the proteins of Watson et al. because Watson et al. teach their agents for targeting the blood pool and because of the expectation of achieving a stable contrast agent that is able to locate harmful fibrin blood clots.

Furthermore, the claims are directed to a method of administering to a patient an effective amount of a detectable reagent comprising discrete particles dispersed in a pharmaceutically or veterinarily acceptable carrier, diluent, excipient, adjuvant or any combination thereof, wherein said particles comprise a detectable marker encased in at least two layers of carbon, wherein the outer surface of said particles allows for a stable chemical association with an aqueous medium and wherein upon administration of said reagent said particles are dispersed in the aqueous medium and form a stable colloid; binding said particles to said fibrin; and detecting the presence of said detectable marker in said patient. Any properties exhibited by or benefits provided the composition are inherent and are not given patentable weight over the prior art. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP

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2112.01. The burden is shifted to Applicant to show that the prior art product does not inherently possess the same properties as instantly claimed product. The prior art teaches administration to a patient of compositions containing the same components as instantly claimed, which would inherently detect fibrin in the bloodstream or blood vessel as instantly claimed. Applicant has not provided any evidence of record to show that the prior art compositions do not exhibit the same properties as instantly claimed.

It is respectfully pointed out that it would have been obvious to one of ordinary skill in the art to hydrolyze the outer layer of the graphite particle because of the expectation of achieving a product that is soluble in its delivery medium.

It is further respectfully pointed out that a compound and its properties are inseparable. Thus, while not explicitly stated, the graphitic carbon of Watson must have the property of stably associating with an aqueous medium.

The Examiner respectfully points out instant claims 82-83 are product-by-process claims. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

Claim 64 is rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. in view of The Handbook of Carbon, Graphite, Diamond, and Fullerenes, and in view of Reno et al.

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as applied to claims 31, 33, 34, 61, 71, 80-83 above, and further in view of The Handbook of Cosmetic Science and Technology.

Watson et al., The Handbook, and Reno et al. fail to teach nanocolloids.

The Handbook of Cosmetic Science and Technology teaches the surface chemistry of colloid systems. It is taught that a reduction in size of the dispersed phase particles increases the stability of the colloid. See pages 67-69.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the dispersion of the combined references as a nanodispersion, wherein a dispersion is a form of a colloid, because of the expectation of achieving a more stable formulation.

Claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. in view of The Handbook of Carbon, Graphite, Diamond, and Fullerenes, and in view of Reno et al. as applied to claims 31, 33, 34, 61, 71, 80-83 above, and further in view of Park et al. (5,330,768) and Penfold et al. (J. Phys. Chem.).

Watson, The Handbook, and Reno et al. are applied as discussed above. The reference lacks C16EO6.

Park et al. teach films for drug delivery comprised of poly(lactic acid) and polyethyleneoxide and polypropylene oxide. It is taught that the water content of the polymer can be controlled by blending different kinds of block polymers and by adjusting ratios. These compounds also exhibit a wide range of hydrophilicity/hydrophobicity. See Col. 3, line 4-line 50.

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Penfold et al. teach C16EO6 as a known, beneficial nonionic polyethylene oxide surfactant. See abstract and page 18133.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the polymers taught by Park et al. as the alkyl alkoxyated surfactants of the combined references because a) Park et al.'s surfactants are alkyl alkoxyated and because of the expectation of achieving a contrast agent particle compound whose hydrophilicity/hydrophobicity can be altered.

While Park et al. does not specifically teach the empirical formula C16EO6, the Examiner respectfully points out that it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233. Thus, one of skill in the art would be motivated to alter the chain length of the polyethyleneoxide to obtain a surfactant with beneficial solubility properties, so as to obtain a surfactant as taught by Penfold et al.

Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Watson et al. in view of The Handbook of Carbon, Graphite, Diamond, and Fullerenes and in view of Reno et al. as applied to claims 31, 33, 34, 61, 71, 80-83 above, and further in view of Doherty et al. (5,952,321).

Watson, The Handbook, and Reno et al. are applied as discussed above. The reference lacks glucose in water.

Doherty et al. teach water, Ringer's solution, glucose in water, and isotonic sodium chloride, as acceptable vehicles for in vivo administration of active agents. See Col. 18, line 57-Col. 19, line 9.

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the glucose in water, taught by Doherty et al., for the vehicles taught by the combined references because the combined references water, sodium chloride injections, and Ringer's solution as interchangeable vehicles, and Doherty et al. teach water-in-glucose as an interchangeable vehicle with water, sodium chloride injections, and Ringer's solution. Thus, substituting one for the other would be expected to achieve similar vehicle effects.

While Doherty et al. does not teach the glucose in an amount of 5%, it is respectfully pointed out that it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233. Furthermore, one of skill in the art would be motivated to adjust the amount of glucose to be compatible with the physiological environment of the body.

Response to Arguments

Applicant's arguments are directed toward the fullerene disclosure in Watson et al. The new rejection above, necessitated by Applicant's amendments to the claims, is directed toward the disclosure of graphitic carbon in Watson et al. Since Applicant has not addressed the disclosure of graphitic carbon in Watson et al., the instant arguments are moot.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO**

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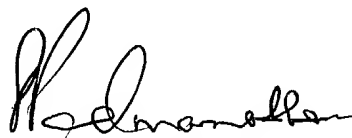
MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is 571-272-0634. The examiner can normally be reached on M&R (5:30-4).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

lqw


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